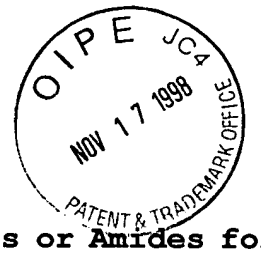
PATENT
Attorney Docket No. 23138S

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Ross, et al.



Serial No.: 09/134,419 Group Art Unit: 1614

Filed: August 14, 1998

For: **Heterocyclic Esters or Amides for Vision and Memory Disorders**

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Pursuant to Applicants' duty of disclosure under 37 C.F.R. §§ 1.56 and 1.97-1.99, the documents listed on the attached Form PTO-1449 are being brought to the attention of the Examiner in charge of the captioned application. No fee is required for this submission because it is submitted within three months from the filing date or before a First Office Action on the merits has been mailed by the U.S. Patent and Trademark Office (USPTO).

A completed Form PTO-1449 is attached hereto. Copies of the cited references are concurrently filed with the Information Disclosure Statement in U.S. Patent Application No. 09/134,422, pursuant to agreement with Examiner Zohreh Fay, Art Group 1614. If additional copies of the references cited herein are required, kindly telephone the undersigned attorney. The Examiner is respectfully requested to cite the documents listed on the attached Form PTO-1449 in the next Office Action. In so doing, the Examiner

is respectfully requested to initial in the space adjacent to the listing of each document on the Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicants, to confirm that these documents have been considered by the Examiner and made of record in this application.

If the Examiner has any questions or wishes to discuss this application, kindly telephone the undersigned attorney.

Respectfully submitted,

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Date: November 16, 1998

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FORM PTO-1449 INFORMATION DISCLOSURE CITATION	Attorney Docket 23138S	Serial Number 09/134,419
	Applicant Ross, et al.	
	Filing Date August 14, 1998	Group Art Unit 1614

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	AA	5,703,088	12/30/97	Sharpe et al.			6/4/92
	AB	5,631,017	5/20/97	Sharpe et al.			3/26/93
	AC	5,614,547	3/25/97	Hamilton et al.			6/7/95
	AD	5,543,423	8/6/96	Zelle et al.			1/23/95

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	AE	DE4015255	11/14/91	Germany			No
	AF	DE3931051	3/29/90	Germany			No
	AG	DE3508251	9/11/86	Germany			No
	AH	EP-652229	5/10/95	EPO			Yes
	AI	EP-572365	12/1/93	EPO			Yes
	AJ	EP-468339	1/29/92	EPO			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AK		Ando, Takao et al., "Formation of Crossed Phenzine from the Reaction between Tetra-p-anisyl- and Tetra-p-tolyl-hydrazines in Liquid Sulphur Dioxide," Chem. Comm., S. Chem. Comm., 1975, 989.
	AL		Andrus, Merrit B., "Structure-based design of an acyclic ligand that bridges FKBP12 and calcineurin," J. Am. Chem. Soc., 1993, 115(2), 10420-1.
	AM		Armistead, D.M. et al., "Design, synthesis and structure of non-macrocyclic inhibitors of FKBP12, the major binding protin for the immunosuppressant FK506," Acta Crystallogr. 1995, D51(4), 522-8.
	AN		Askin, D. et al., "Chemistry of FK-506: benzilic acid rearrangement of the tricarbonyl system," Tetrahedron Lett., 1989, 30(6), 671-4.
	AO		Askin, D. et al., "Effecient Degradation of FK-506 to a versatile synthetic intermediate," J. Org. Chem., 1990, 55(20), 5451-4.
	AP		Baader, Ekkehard et al., "Inhibition of prolyl 4-hydroxylase by oxalyl amino acid derivatives in vitro, in isolated microsomes and in embryonic chicken tissues," Biochem. J., 1994, 300(2), 525-30.

Examiner	Date Considered

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Draw line through citation if not in conformance and not considered.
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	BA	5,516,797	5/14/96	Armistead et al.			4/11/94
	BB	5,447,915	9/5/95	Schreiber et al.			8/28/92
	BC	5,424,454	6/13/95	Burbaum, B.W. et al.			5/26/94
	BD	5,414,083	5/9/95	Hackl et al.			1/24/94

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	BE	EP-419049	3/27/91	EPO			Yes
	BF	EP-405994	1/2/91	EPO			Yes
	BG	EP-378318	7/18/90	EPO			Yes
	BH	EP-352000	1/24/90	EPO			Yes
	BI	EP-333174	9/20/89	EPO			Yes
	BJ	EP-260118	3/16/88	EPO			Yes
	BK	EP-196841	10/8/86	EPO			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	BL		Baumann, K. et al., "Synthesis and oxidative cleavage of the major equilibrium products of ascomycin and Fk 506," Tetrahedron Lett., 1995, 26(13), 2231-4.
	BM		Bender, D., et al., "Periodate oxidation of α-keto γ-lactams. Enol oxidation and β-lactam formation. Mechanism of periodate hydroxylation reactions," J. Org. Chem., 1978, 43(17), 3354-62.
	BN		Birkenshaw, T.N. et al., "Synthetic FKBP12 Ligands. Design and Synthesis of Pyranose Replacements," Bioorganic & Medicinal Chemistry Letters, (1994) 4:21, 2501-2506.
	BO		Boulmedais, Ali et al., "Stereochemistry of Electrochemical Reduction of Optically Active α-ketoamides. II. Electroreduction of benzoylformamides derived from S-(-)-proline," Bull. Soc. Chim. Fr., 1989, (2), 185-91. (French)
	BP		Cameron, Andrew et al., "Immunophilin FK506 binding protein associated with inositol 1,4,5-triphosphate receptor modulates calcium flux," Proc. Natl. Acad. Sci. USA, 1995, 92, 1784-1788.
	BQ		Caufield, Craig E. and Musser, John H., "Macrocyclic Immunomodulators," Annual Reports in Medicinal Chemistry, Johns (Ed.), Academic Press, Chapter 21, 195-204, 1989.

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Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	CA	5,359,138	10/25/94	Takeuchi et al.			6/29/92
	CB	5,330,993	7/19/94	Armistead et al.			7/2/91

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	CC	EP--88350	9/14/83	EPO			Yes
	CD	EP--73143	3/2/83	EPO			Yes

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	CE		Caffrey, M.V. et al., "Synthesis and Evaluation of Dual Domain Macrocyclic FKBP12 Ligands," Bioorganic & Medicinal Chemistry Letters, (1994) 4:21, 2507-2510.
	CF		Chakraborty, TK et al., "Design and Synthesis of a rapamycin-based high affinity binding FKBP12 ligand," Chem. Biol., 1995, 2(3), 157-61.
	CG		Chakaraborty, Tushar K., "Studies towards the development of cyclic peptide-based analogs of macrolide immunosuppressants," Pure Appl. Chem., 1996, 68(3), 565-568.
	CH		Coleman, R., and Danishefsky, S., "Degradation and manipulations of the immunosuppressant FK506: preparation of potential synthetic intermediates," Heterocycles, 1989, 28(1), 157-61.
	CJ		Colombo, L. et al., "Enantioselective synthesis of secondary alcohols in the presence of chiral ligands," Tetrahedron, 1982, 38(17), 2725-7.
	CK		Cunliffe, C. Jane et al., "Novel inhibitors of prolyl 4-hydroxylase. 3. Inhibition by the substrate analog N-oxaloglycine and its derivatives," J. Med. Chem., 1992, 35 (14), 2652-8.
	CL		Cushman, D.W. et al., "Design of potent competitive inhibitors of angiotensin-converting enzyme. Carboxyalkanoyl and mercaptoalkanoyl amino acids," Biochemistry, 1977, 16(25), 5484-91.
	CM		Dawson, Ted M. et al., "Immunosuppressant FK506 enhances phosphorylation of nitric oxide synthase and protects against glutamate neurotoxicity," Proc. Natl. Acad. Sci. USA, 1993, 90, 9808-12.
	CN		Dawson, T.M. et al., "The immunophilins, FK506 binding and cyclophilin, are discretely localized in the brain: relationship to calcineurin," Neuroscience, 1994, 62(2), 569-80.

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	DA	5,319,098	6/7/94	Burbaum, B.W. et al.			5/26/94
	DB	5,294,603	3/15/94	Rinehart, K.L.			2/18/92

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	DC	EP--50800	5/5/82	EPO			Yes
	DD	EP--48159	3/24/82	EPO			Yes
	DE	EP--12401	6/25/80	EPO			Yes
	DF	GB2247456	3/4/92	United Kingdom			Yes
	DG	JP05178824	7/20/93	Japan			No

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	DG		Effenberger F. et al., "Diastereoselective addition of benzenesulfenyl chloride to 1-acryloylproline esters," Chemical Abstracts, 1989, 110:154846h.
	DH		Egbertson, M. and Danishefsky, S., "A synthetic route to the tricarbonyl region of FK-506," J. Org. Chem., 1989, 54(1), 11-12.
	DI		Feutren, Gilles, "The Optimal use of Cyclosporin A in Autoimmune Diseases," J. of Autoimmunity, 1992, 5, 183-95.
	DJ		Finberg, Robert W. et al., "Prevention of HIV-1 Infection and Preservation of CD4 Function by the Binding of CPFs to gp120," Science, 1990, 249, 287-91.
	DK		Fisher, Matthew et al., "On the remarkable propensity for carbon-carbon bond cleavage reactions in teh C(8)-C(10) region of FK-506," J. Org. Chem., 1991, 56(8), 2900-7.
	DL		Fry, Lionel, "Psoriasis: Immunopathology and Long-term treatment with Cyclosporin," J. of Autoimmunity, 1992, 5, 277-83.

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	EA	5,252,579	10/12/93	Skotnicki et al.			2/16/93
	EB	5,147,877	9/15/92	Goulet			9/12/91

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	EC	JP04149166	5/22/92	Japan			No
	ED	WO9824805	6/11/98	PCT			Yes
	EE	WO9820893	5/22/98	PCT			Yes

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	EF		Furber, Mark, "FKBP-12-ligand-calceineurin interactions: analogs of SBL506," J. Am. Chem. Soc., 1995, 117(27), 7267-8.
	EG		Furber, M. et al., "Studies relating to the immunosuppressive activitiy of FK506," Tetrahedron Lett., 1993, 34(8), 1351-4.
	EH		Goodfellow, Val S. et al., "p-Nitrophenyl 3-diazopyruvate and diazopyruvamides, a New Family of Photoactivatable Cross-Linking Bioprobes," Biochemistry, 28(15), 6346-60.
	EI		Goulet, Mark T., and Boger, Joshua, "Degradative studies on the tricarbonyl containing macrolide rapamycin," Tetrahedron Lett., 1990, 31(34), 4845-8.
	EJ		Goulet, Mark T. and Boger, Joshua, "Degradative studies on the tricarbonyl containing macrolide rapamycin," Tetrahedron Lett., 1991, 32(45), 6454.
	EK		Haeusler, Johannes and Schmidt, Ulrich, "Amino acids and peptides. IX. Pyruv oyl amino acids," Chem. Ber., 1974, 107(1), 145-51. (German)
	EL		Harding, M.W., et al., "A receptor for the immunosuppressant FK506 is a *cis-trans* peptidyl-prolyl isomerase," Nature Lett., 1989, 341, 758-60.
	EM		Hauske, J.R. et al. "Design and Synthesis of Novel FKBP Inhibitors," J. of Medicinal Chemistry, (1992) 35, 4284-4296.
	EN		Hauske, James R. et al., "Investigation of the effects of synthetic, non-cytotoxic immunophilin inhibitors on MDR," Bioorg. Med. Chem.. Lett., 1994, 4(17), 2097-102.
	EO		Hayward, C.M. et al., "Total Synthesis of rapamycin via a novel titanium-mediated aldol macrocyclization reaction," J. Am. Chem. Soc., 1993, 115(20), 9345-6.
	EP		Hayward, C.M. et al., "An application of the Suarez reaction to the regiospecific synthesis of the C_{28}-C_{42} segment of rapamycin," 3989-92.

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	FA	4,818,749	4/4/89	Gold, E.H. et al.			4/4/89
	FB	4,808,573	2/28/89	Gold, E.H. et al.			2/28/89

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		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	FC	WO9820892	5/22/98	PCT			Yes
	FD	WO9820891	5/22/98	PCT			Yes
	FE	WO9636630	11/21/96	PCT			Yes
	FF	WO9633187	10/24/96	PCT			Yes
	FG	WO9633184	10/24/96	PCT			Yes
	FH	WO9617816	6/13/96	PCT			Yes
	FI	WO9615101	5/23/96	PCT			Yes
	FJ	WO9606097	2/29/96	PCT			Yes
	FK	WO9603318	10/24/96	PCT			Yes
	FL	WO9535367	12/28/95	PCT			Yes
	FM	WO9535308	12/28/95	PCT			Yes

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	FN		Holt, D.A. et al., "Design, Synthesis, and Kinetic Evaluation of High-Affinity FKBP Ligands and the X-ray Crystal Structures of Their Complexes with FKBP12," J. Am. Chem. Soc., (1993) 115, 9925-9938.
	FO		Holt, D.A. et al., "Structure-Activity Studies of Nonmacrocyclic Rapamycin Derivatives," Bioorganic & Medicinal Chemistry Letter, (1993) 3:10, 1977-1980.
	FP		Holt, D.A. et al., "Structure-Activity Studies of Synthetic FKBP Ligands as Peptidyl-prolyl Isomers Inhibitors," Bioorganic & Medicinal Chemistry Letters, (1994) 4:2, 315-320.
	FQ		Hearn, Walter R., and Worthington, Robert E., "L-Proline-N-oxalic anhydride," J. Org. Chem., 1967, 32(12), 4072-4.
	FR		Iwabuchi, T. et al., "Effects of immunosuppressive peptidyl-prolyl cis-trans isomerase (PPIase inhibitors, cyclosporin A, FK506, ascomycin and rapamycin, on hair growth initiation in mouse: immunosuppression is not required for hair growth," J. of Deramatol. Sci., (1995) 9:1, 64-69.
	FS		Jiang, H. et al., "Induction of anagen in telogen mouse skin by topical application of FK506, a potent immunosuppressant," J. Invest. Dermatol., (1995) 104:4, 523-525.
	FT		Jones, T. et al., "Chemistry of tricarbonyl hemiketals and application of Evans technology to the total synthesis of the immunosuppressant (-)-FK-506," J. Am. Chem. Soc., 1990, 112(8), 2998-3017.
	FU		Jones, A. et al., "A formal synthesis of FK-506. Exploration of some alternatives to macrolactamization," J. Org. Chem., 1990, 55(9), 2786-97.

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	GA	4,593,102	6/3/86	Shanklin Jr.			7/1/95
	GB	4,578,474	3/25/86	Krapcho et al.			11/19/84

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	GC	WO9526337	10/5/95	PCT			Yes
	GD	WO9524385	9/14/95	PCT			Yes

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	GE		Kaczmar, et al., Makromol. Chem., 1976, 177, 1981-9 (German).
	GF		Karle, Isabella L. et al., "Coformation of the oxalamide group in retro-bispeptides. Three crystal structures," Int. J. Pept. Protein Res., 1994, 43(2), 160-5.
	GG		Kino, Toru et al., "FK-506, A novel immunosuppressnt isolateded from A streptomyces," J. of Antibiotics, 1987, 40(9), 1249-55.
	GH		Kocienski, P. et al., "A synthesis of the C(1)-C(15) segment of tsukubaenolide (FK506)," Tetrahedron Lett., 1988, 29(35), 4481-4.
	GI		Krit, N.A. et al., "Impact of the nature of alkyl radical on the biological activity of N-carboxyalkyl dipeptides," Khim.-Farm. Zh., 1991, 25(7), 44-6. (Russian)
	GJ		Linde, Robert G. et al., "Straightforward synthesis of 1,2,3-tricarbonyl systems," J. Org. Chem., 1991, 56(7), 2534-8.
	GK		Luengo, Juan I. et al., "Efficient removal of pipecolinate from rapamycin and FK506 by reaction with tetrabutylammonium cyanide," Tetrahedron Lett., 1993, 34(29), 4599-602.
	GL		Luengo, J. et al., "Studies on the chemistry of rapamycin: novel transformation under Lewis-acid catalysis," Tetrahedron Lett., 1993, 34(6), 991-4.
	GM		Luengo, J.I. et al., "Synthesis and Structure-Activity Relationships of Macrocyclic FKBP Ligands," Bioorganic & Medicinal Chemistry Letters, (1994) 4:2, 321-324.
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	GO		Lyons, W. Ernest et al., "Neronal Regeneration Enhances the Expression of the Immunophilin FKBP-12," The Journal of Neuroscience, 1995, 15, 2985-94.

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	HA	4,574,079	3/4/86	Gavras, H.P. et al.			3/4/86
	HB	4,531,964	7/30/85	Shimano et al.			8/29/83

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	HC	WO9512572	5/11/95	PCT			Yes
	HD	WO9413629	6/23/94	PCT			Yes

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	HE		Marshall, J.A. et al., "Convenient synthesis of dioxopiperazines via aminolysis of .alpha.-(pyruvylamino) esters, Synth. Commun., 1975, 5(3), 237-44.
	HF		Mashkovskii, M.D. et al., "1-[4-(2-Hydroxy-3-tert-butylaminopropoxy)-indole-3-yl (5-acetamido-1-(S)-carboxypentyl)-DL-alanyl]-L-proline dihydrochloride, a new angiotensin-converting enzyme inhibitor with β-adrenoblocking properties," Khim.-Farm. Zh., 1993, 27(10), 16-20. (Russian)
	HG		Munegumi, Toratane et al., "Asymmetric Catalytic Hydrogenations of N-pyruvoyl-(S)-proline esters," Bull. Chem. Soc. Jpn., 1987, 60(1), 243-53.
	HH		Munoz, Benito et al., "α-Ketoamide Phe-Pro isostere as a new core structure for the inhibition of HIV protease," Bioorg. Med. Chem., 1994, 2(10), 1085-90.
	HI		Nakatsuka, M et al. " Total Synthesis of FK506 and an FKBP Reagent, (C_8, C_9- $^{13}C_2$)-FK-506," J. Am. Chem. Soc., 1990, 112 (14), 5583-90..
	HJ		Nelson, F. et al., "A novel ring contraction of rapamycin," Tetrahedron Lett., 1994, 35(41), 7557-60.
	HK		Nicolaou, K.C. et al., "Total Synthesis of rapamycin," J. Am. Chem. Soc., 1993, 115(10), 4419-20.
	HL		Pattenden, Gerald and Tankard, Mark, "Facile Synthesis of the tricarbonyl subunit in the immunosuppressant rapamycin," Tetrahedron Lett., 1993, 34(16), 2677-80.
	HM		Ponticelli, Claudio, "Treatment of the Nephrotic Syndrome with Cyclosporin A," J. of Autoimmunity, 1992, 5, 315-24.
	HN		Ranganathan, Darshan et al., "Protein Backbone Modification by Novel Cα-C Side-Chain Scission," 1994, J. Am. Chem. Soc., 116(15), 6545-57.

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	IA	4,390,695	1/28/83	Krapcho et al.			6/1/81
	IB	4,374,829	2/22/83	Harris, E., et al.			2/22/83
	IC	4,310,461	1/12/82	Krapcho et al.			1/23/80
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	IE	WO9407858	4/14/94	PCT			Yes
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	IG		Rao, A.V., et al., "Studies directed towards the synthesis of immunosuppressive agent FK-506: construction of the tricarbonyl moiety," Tetrahedron Lett., 1990, 31(10), 1439-42.
	IH		Rao, A.V. Rama et al., "Studies directed towards the synthesis of immunosuppressive agent FK-506: synthesis of the entire bottom half," Tetrahedron Lett., 1991, 32(9), 1251-4.
	II		Rao, A.V. Rama and Desibhatla, Vidyanand, "Studies directed towards the syntesis of rapamycin: stereoselective synthesis of C-1 to C-15 segment," Tetrahedron Lett., 1993, 34(44), 7111-14.
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	IK		Skotnicki, Jerauld et al., "Ring expanded rapamycin derivatives," Tetrahedron Lett., 1994, 35(2), 201-2.
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FORM PTO-1449 INFORMATION DISCLOSURE CITATION	Attorney Docket 23138S	Serial Number 09/134,419
	Applicant Ross, et al.	
	Filing Date August 14, 1998	Group Art Unit 1614

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	JA						

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		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	JB	WO9325546	12/23/93	PCT			Yes
	JC	WO9323548	11/15/93	PCT			Yes

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	JE		Soai, Kenso and Hasegawa, Hitoshi, "Diastereoselective reduction of chiral α-ketoamides derived from (S)-proline esters with sodium borohydride. Preparation of optically active α-hydroxy acids," J. Chem. Soc., 1985, 1(4), 769-72.
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	KA						

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		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	KB	WO9313066	7/8/93	PCT			Yes
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	LA						

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		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	LB	WO9221313	12/10/92				
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	LD		Wang, C.P. et al., "A high performance liquid chromatographic method for the determination of rapamycin {sirolimus} in rat serum, plasma, and blood and in monkey serum," J. Liq. Chromatogr., 1995, 18(9), 1801-8.
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U.S. PATENT DOCUMENTS

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	MA						
	MB						

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	MC	WO9219593	11/12/92	PCT			Yes
	MD	WO9218478	10/29/92	PCT			Yes
	ME	WO9216501	10/1/92	PCT			Yes
	MF	WO9204370	3/19/92	PCT			Yes
	MG	WO9203472	3/5/92	PCT			Yes
	MH	WO9200278	1/9/92	PCT			Yes
	MI	WO9113088	9/5/91	PCT			Yes
	MJ	WO9104985	4/18/91	PCT			Yes
	MK	WO9012805	11/1/90	PCT			Yes
	ML	WO8809789	12/15/88	PCT			Yes
	MM	ZA9207782	4/28/93	South Africa			Yes

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